

## General

### Guideline Title

Practice parameter update: management issues for women with epilepsy--focus on pregnancy (an evidence-based review): vitamin K, folic acid, blood levels, and breastfeeding. Report of the Quality Standards Subcommittee and Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and American Epilepsy Society.

### Bibliographic Source(s)

Harden CL, Pennell PB, Koppel BS, Hovinga CA, Gidal B, Meador KJ, Hopp J, Ting TY, Hauser WA, Thurman D, Kaplan PW, Robinson JN, French JA, Wiebe S, Wilner AN, Vazquez B, Holmes L, Krumholz A, Finnell R, Shafer PO, Le Guen C. Practice parameter update: management issues for women with epilepsy--focus on pregnancy (an evidence-based review): vitamin K, folic acid, blood levels, and breastfeeding. Report of the Quality Standards Subcommittee [trunc]. *Neurology*. 2009 Jul 14;73(2):142-9. [45 references] [PubMed](#)

### Guideline Status

This is the current release of the guideline.

The American Academy of Neurology reaffirmed the currency of this guideline in 2016.

This guideline meets NGC's 2013 (revised) inclusion criteria.

## Recommendations

### Major Recommendations

Definitions of the levels of the recommendations (A, B, C, U) and classification of the evidence (Class I-IV) are provided at the end of the "Major Recommendations" field.

Does preconceptional folic acid supplementation reduce the risk of birth defects in neonates of women with epilepsy (WWE) taking antiepileptic drugs (AEDs)?

#### *Conclusions*

- The risk of major congenital malformations (MCMs) in the offspring of women with epilepsy (WWE) is possibly decreased by folic acid supplementation (two adequately sensitive Class III studies).

#### *Recommendations*

- Preconceptional folic acid supplementation in WWE may be considered to reduce the risk of major congenital malformations (MCMs) (Level C).

What is the risk of hemorrhagic disease in neonates born to WWE taking AEDs?

#### *Conclusion*

- There is insufficient evidence to determine if the risk of neonatal hemorrhagic complications in the newborns of WWE taking AEDs is substantially increased (one inadequately sensitive Class II study).

#### *Recommendation*

- Counseling of WWE who are pregnant or are contemplating pregnancy should reflect that there is insufficient evidence to support or refute an increased risk of hemorrhagic complications in the newborns of WWE taking antiepileptic drugs (AEDs) (Level U).

Does prenatal vitamin K supplementation reduce the risk of hemorrhagic complications in the newborns of WWE taking AEDs?

#### *Conclusion*

- Evidence is inadequate to determine if prenatal vitamin K supplementation in WWE reduces neonatal hemorrhagic complications.

#### *Recommendation*

- There is insufficient evidence to support or refute a benefit of prenatal vitamin K supplementation for reducing the risk of hemorrhagic complications in the newborns of WWE (Level U).

Do maternally ingested AEDs cross the placenta? Do maternally ingested AEDs penetrate into breast milk?

#### *Conclusions (Placental Transfer)*

- Phenobarbital (PB), primidone (PRM), phenytoin (PHT), carbamazepine (CBZ), levetiracetam (LVT), and valproate (VPA) probably cross the placenta in potentially clinically important amounts (one Class I and supporting Class II studies or two or more Class II studies).
- Gabapentin (GBP), lamotrigine (LTG), oxcarbazepine (OXC), and topiramate (TPM) possibly cross the placenta in potentially clinically important amounts (at least one Class II study for each).
- There are insufficient data to determine if ethosuximide (ESM) crosses the placenta in clinically important amounts (one Class III study showing significant penetration).

#### *Recommendation (Placental Transfer)*

- The fact that PB, PRM, PHT, CBZ, LVT, VPA, GBP, LTG, OXC, and TPM cross the placenta may be factored into the clinical decision regarding the necessity of AED treatment for a woman with epilepsy (Level B for PB, PRM, PHT, CBZ, LVT, and VPA, and Level C for GBP, LTG, OXC, and TPM).

#### *Conclusions (Breast Milk Penetration)*

- PRM and LVT probably penetrate into breast milk in potentially clinically important amounts (one Class I study and a supporting Class II study or two Class II studies).
- GBP, LTG, and TPM possibly penetrate into breast milk in potentially clinically important amounts (one Class II study each).
- VPA, PB, PHT, and CBZ probably do not penetrate into breast milk in potentially clinically important amounts (one Class I study and a supporting Class II study or two Class II studies).
- There are insufficient data to determine if ESM penetrates into breast milk in clinically important amounts (one Class III study showing significant transfer).

#### *Recommendation (Breast Milk Penetration)*

- VPA, PB, PHT, and CBZ may be considered as not transferring into breast milk to as great an extent as PRM, LVT, GBP, LTG, and TPM (Level B when compared to PRM and LVT and Level C when compared to GBP, LTG, and TPM).

Does indirect exposure to maternally ingested AEDs lead to symptomatic effects in the newborn?

#### *Conclusion*

- There is no evidence to determine if indirect exposure to maternally ingested AEDs has symptomatic effects on the newborns of WWE.

#### *Recommendation*

- None (Level U)

For each of the AEDs, does pregnancy cause a change in the levels of the medication or clearance of the medication?

### *Conclusions*

- Pregnancy probably causes an increase in the clearance and a decrease in the level of LTG during pregnancy. The decrease in LTG level is associated with an increase in seizure frequency (one Class I and two Class II studies)
- Pregnancy probably causes a small decrease in concentration of CBZ (9% in second trimester and 12% in third trimester) (one Class I study).
- Pregnancy probably causes an increase in the clearance and a decrease in the level of PHT during pregnancy (one Class I study).
- Pregnancy possibly causes a decrease in the level of the active OXC metabolite, monohydroxy derivative (MHD) (two Class III studies).
- Pregnancy possibly causes a decrease in the level of LVT (one Class II study).
- Evidence for a change in clearance or level of PB, VPA, PRM, and ESM during pregnancy is inadequate to reach a conclusion.

### *Recommendations*

- Monitoring of LTG, CBZ, and PHT levels during pregnancy should be considered (Level B).
- Monitoring of LVT and OXC (as MHD) levels during pregnancy may be considered (Level C).
- There is insufficient evidence to support or refute a change in PB, VPA, PRM, or ESM levels related to pregnancy (Level U), and this lack of evidence should not discourage monitoring levels of these AEDs during pregnancy.

### Definitions:

#### Classification of Recommendations

The strength of practice recommendations is linked directly to the level of evidence:

Level A = Established as effective, ineffective, or harmful (or established as useful/predictive or not useful/predictive) for the given condition in the specified population. (Level A rating requires at least two consistent Class I studies.\*)

Level B = Probably effective, ineffective, or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified population. (Level B rating requires at least one Class I study or two consistent Class II studies.)

Level C = Possibly effective, ineffective, or harmful (or possibly useful/predictive or not useful/predictive) for the given condition in the specified population. (Level C rating requires at least one Class II study or two consistent Class III studies.)

Level U = Data inadequate or conflicting; given current knowledge, treatment (test, predictor) is unproven.

\*In exceptional cases, one convincing Class I study may suffice for an "A" recommendation if: 1) all criteria are met, 2) the magnitude of effect is large (relative rate improved outcome >5 and the lower limit of the confidence interval is >2).

#### Classification of Evidence for Rating of a Prognostic Article

Class I = A cohort study of a broad spectrum of persons at risk for developing the outcome (e.g., target disease, work status). The outcome is defined by an acceptable reference standard for case definition. The outcome is objective or measured by an observer who is masked to the presence of the risk factor. Study results allow calculation of measures of prognostic accuracy.

Class II = A case control study of a broad spectrum of persons with the condition compared to a broad spectrum of controls or a cohort study of a broad spectrum of persons at risk for the outcome (e.g., target disease, work status) where the data was collected retrospectively. The outcome is defined by an acceptable reference standard for case definition. The outcome is objective or measured by an observer who is masked to the presence of the risk factor. Study results allow calculation of measures of prognostic accuracy.

Class III = A case control study or a cohort study where either the persons with the condition or the controls are of a narrow spectrum where the data was collected retrospectively. The outcome is defined by an acceptable reference standard for case definition. The outcome is objective or measured by an observer who did not determine the presence of the risk factor. Study results allow calculation of measures of a prognostic accuracy.

Class IV = Studies not meeting Class I, II, or III criteria including consensus, expert opinion or a case report.

#### Classification of Evidence for Studies of Therapeutic Intervention

Class I = A randomized, controlled clinical trial of the intervention of interest with masked or objective outcome assessment, in a representative population. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences. The following are also required:

- a. Concealed allocation
- b. Primary outcome(s) clearly defined
- c. Exclusion/inclusion criteria clearly defined
- d. Adequate accounting for drop-outs (with at least 80% of enrolled subjects completing the study) and cross-overs with numbers sufficiently low to have minimal potential for bias
- e. For non-inferiority or equivalence trials claiming to prove efficacy for one or both drugs, the following are also required\*:
  1. The authors explicitly state the clinically meaningful difference to be excluded by defining the threshold for equivalence or non-inferiority.
  2. The standard treatment used in the study is substantially similar to that used in previous studies establishing efficacy of the standard treatment. (e.g., for a drug, the mode of administration, dose and dosage adjustments are similar to those previously shown to be effective).
  3. The inclusion and exclusion criteria for patient selection and the outcomes of patients on the standard treatment are comparable to those of previous studies establishing efficacy of the standard treatment.
  4. The interpretation of the results of the study is based upon a per protocol analysis that takes into account dropouts or crossovers.

Class II = A randomized controlled clinical trial of the intervention of interest in a representative population with masked or objective outcome assessment that lacks one criteria a–e above or a prospective matched cohort study with masked or objective outcome assessment in a representative population that meets b–e above. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences.

Class III = All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome is independently assessed, or independently derived by objective outcome measurement.\*\*

Class IV = Studies not meeting Class I, II, or III criteria including consensus or expert opinion.

\*Note that numbers 1-3 in Class Ie are required for Class II in equivalence trials. If any one of the three is missing, the class is automatically downgraded to Class III.

\*\*Objective outcome measurement: an outcome measure that is unlikely to be affected by an observer's (patient, treating physician, investigator) expectation or bias (e.g., blood tests, administrative outcome data).

## Clinical Algorithm(s)

None provided

## Scope

## Disease/Condition(s)

Epilepsy plus:

Pregnancy  
Breastfeeding

## Guideline Category

Evaluation

Management

Prevention

Risk Assessment

Treatment

## Clinical Specialty

Family Practice

Neurology

Nursing

Nutrition

Obstetrics and Gynecology

Pediatrics

Pharmacology

## Intended Users

Advanced Practice Nurses

Dietitians

Health Care Providers

Health Plans

Managed Care Organizations

Patients

Pharmacists

Physician Assistants

Physicians

## Guideline Objective(s)

To reassess the evidence for management issues related to the care of women with epilepsy (WWE) during pregnancy, including preconceptional folic acid use, prenatal vitamin K use, risk of hemorrhagic disease of the newborn, clinical implications of placental and breast milk transfer of antiepileptic drugs (AEDs), risks of breastfeeding, and change in AED levels during pregnancy

## Target Population

Women with epilepsy (WWE) who are pregnant, planning pregnancy, or breastfeeding or planning to breastfeed

## Interventions and Practices Considered

Counseling women with epilepsy (WWE) who are planning pregnancy

Preconceptional folic acid supplementation

Antiepileptic drug (AED) blood level monitoring during pregnancy

Note: The effect of prenatal vitamin K supplementation and AEDs on newborns was considered, but insufficient evidence existed for a recommendation to be made.

## Major Outcomes Considered

- Incidence of major congenital malformations (association with preconceptional folic acid use)
- Risk of neonatal hemorrhagic complications
- Antiepileptic drug (AED) levels in neonatal serum and maternal breast milk
- Symptomatic effects in the newborn attributable to AEDs
- Change in serum AED levels during pregnancy

## Methodology

### Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Searches of Electronic Databases

### Description of Methods Used to Collect/Select the Evidence

#### 2009 Guideline

A literature search was performed using MEDLINE, MEDLINE-In-Process, Current Contents, Biologic Abstracts, and BIOSIS previews for relevant articles published between 1985 and December 2005. An updated search was performed from December 2005 through June 2007, with manual searches on some topics through February 2008. The arbitrary cutoff date of 1985 was chosen because these relatively recent articles were thought to reflect current practice and antiepileptic drug (AED) usage patterns and therefore be more applicable and reliable for this assessment than earlier reports. The search terms used were seizures/epilepsy, catamenial epilepsy, pregnancy, anticonvulsants, antiepileptic drugs, teratogenesis, birth defects, pregnancy registry, cognitive outcome, vitamin K, folate/folic acid, breastfeeding, oral contraceptives, polycystic ovary syndrome, hormone replacement therapy, menopause, perimenopause, and fertility. The search was confined to articles using human subjects and included all languages for which there was an abstract in English. A secondary search for missed references was done by reviewing the bibliographies of review articles and meta-analyses identified in the primary search.

The literature search yielded a total of 876 abstracts. To find relevant articles, two panel members screened each of the abstracts. If either panel member thought the article was potentially relevant, the full text was obtained for review. In general, abstracts were excluded from further analysis if they related to eclampsia rather than seizures due to epilepsy, related to basic mechanisms such as teratogenesis or placental AED metabolism, or were unrelated to the questions posed by the panel.

From the abstracts, a total of 285 were selected for complete review. Four panel members reviewed the full text of the articles and identified those that were relevant to each clinical question. Seventy-one relevant articles were identified by the literature search.

#### 2013 Reaffirmation

The guideline developer searched Medline, EMBASE, and Current Contents for studies published between 2009 and 2013 using the following search terms: epilepsy, seizure, women with epilepsy, pregnancy complications, seizure frequency, Vitamin K, folic acid, and breastfeeding.

#### 2016 Reaffirmation

The guideline developer searched Medline for studies published between January 2013 to April 2016, using the following search strategy: (((((((breast feeding) OR lactation) OR nurse)) OR #9) OR Abnormalities, Drug-Induced)) AND Anticonvulsants) AND ((pregnancy) AND (((seizures) OR catamenial epilepsy) OR epilepsy)), Vitamin K, folic acid, and breastfeeding. Inclusion criteria were RCTs, humans only, relevant to clinical questions; exclusion criteria used to screen search results were the same as described in the 2009 published guideline.

### Number of Source Documents

Does preconceptional folic acid supplementation reduce the risk of birth defects in neonates of women with epilepsy (WWE) taking antiepileptic drugs (AEDs)? 5 articles

What is the risk of hemorrhagic disease in neonates born to WWE taking AEDs? 2 articles

Does prenatal vitamin K supplementation reduce the risk of hemorrhagic complications in the newborns of WWE taking AEDs? No articles

Do maternally ingested AEDs cross the placenta? Do maternally ingested AEDs penetrate into breast milk? 19 articles

Does indirect exposure to maternally ingested AEDs lead to symptomatic effects in the newborn? No articles

For each of the AEDs, does pregnancy cause a change in the levels of the medication or clearance of the medication? 31 articles

## Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

### Rating Scheme for the Strength of the Evidence

#### Classification of Evidence for Rating of a Prognostic Article

Class I = A cohort study of a broad spectrum of persons at risk for developing the outcome (e.g., target disease, work status). The outcome is defined by an acceptable reference standard for case definition. The outcome is objective or measured by an observer who is masked to the presence of the risk factor. Study results allow calculation of measures of prognostic accuracy.

Class II = A case control study of a broad spectrum of persons with the condition compared to a broad spectrum of controls or a cohort study of a broad spectrum of persons at risk for the outcome (e.g., target disease, work status) where the data was collected retrospectively. The outcome is defined by an acceptable reference standard for case definition. The outcome is objective or measured by an observer who is masked to the presence of the risk factor. Study results allow calculation of measures of prognostic accuracy.

Class III = A case control study or a cohort study where either the persons with the condition or the controls are of a narrow spectrum where the data was collected retrospectively. The outcome is defined by an acceptable reference standard for case definition. The outcome is objective or measured by an observer who did not determine the presence of the risk factor. Study results allow calculation of measures of a prognostic accuracy.

Class IV = Studies not meeting Class I, II, or III criteria including consensus, expert opinion or a case report.

#### Classification of Evidence for Studies of Therapeutic Intervention

Class I = A randomized, controlled clinical trial of the intervention of interest with masked or objective outcome assessment, in a representative population. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences. The following are also required:

- a. Concealed allocation
- b. Primary outcome(s) clearly defined
- c. Exclusion/inclusion criteria clearly defined
- d. Adequate accounting for drop-outs (with at least 80% of enrolled subjects completing the study) and cross-overs with numbers sufficiently low to have minimal potential for bias
- e. For non-inferiority or equivalence trials claiming to prove efficacy for one or both drugs, the following are also required\*:
  1. The authors explicitly state the clinically meaningful difference to be excluded by defining the threshold for equivalence or non-inferiority.
  2. The standard treatment used in the study is substantially similar to that used in previous studies establishing efficacy of the standard treatment. (e.g., for a drug, the mode of administration, dose and dosage adjustments are similar to those previously shown to be effective).
  3. The inclusion and exclusion criteria for patient selection and the outcomes of patients on the standard treatment are comparable to those of previous studies establishing efficacy of the standard treatment.
  4. The interpretation of the results of the study is based upon a per protocol analysis that takes into account dropouts or crossovers.

Class II = A randomized controlled clinical trial of the intervention of interest in a representative population with masked or objective outcome assessment that lacks one criteria a–e above or a prospective matched cohort study with masked or objective outcome assessment in a

representative population that meets b–e above. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences.

Class III = All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome is independently assessed, or independently derived by objective outcome measurement.\*\*

Class IV = Studies not meeting Class I, II, or III criteria including consensus or expert opinion.

\*Note that numbers 1-3 in Class Ie are required for Class II in equivalence trials. If any one of the three is missing, the class is automatically downgraded to Class III.

\*\*Objective outcome measurement: an outcome measure that is unlikely to be affected by an observer's (patient, treating physician, investigator) expectation or bias (e.g., blood tests, administrative outcome data).

## Methods Used to Analyze the Evidence

### Systematic Review with Evidence Tables

## Description of the Methods Used to Analyze the Evidence

### Panel Selection

A 20-member committee evaluated the available evidence based on a structured literature review and classification of relevant articles published between 1985 and October 2007.

### Study Classification and Measures of Effect

Articles were classified according to the American Academy of Neurology (AAN) classification of evidence schemes for prognostic articles and therapeutic intervention studies (see the "Rating Scheme for the Strength of the Evidence" field). Articles were classified separately by four panel members. Disagreements on categorization of the articles were resolved by discussion and consensus.

### Analysis of Evidence

*Does preconceptional folic acid supplementation reduce the risk of birth defects in neonates of WWE taking AEDs?* To be included in the analysis, articles had to measure the association between preconceptional folic acid use and the outcome of major congenital malformations (MCMs).

*What is the risk of hemorrhagic disease in neonates born to WWE taking AEDs?* To be included in the analysis, studies had to compare the risk of neonatal hemorrhagic complications in newborns of WWE taking AEDs to newborns of women without epilepsy.

*Do maternally ingested AEDs cross the placenta? Do maternally ingested AEDs penetrate into breast milk?* Articles were included if the investigators measured AED levels in at least five mother-child pairs for evaluation of placental transfer and a minimum of five maternal serum-breast milk pairs.

*For each of the AEDs, does pregnancy cause a change in the levels of the medication or clearance of the medication?* Articles were included in the analysis if the investigators compared preconception and postpartum AED levels.

## Methods Used to Formulate the Recommendations

### Expert Consensus

## Description of Methods Used to Formulate the Recommendations

### 2009 Guideline

The American Academy of Neurology (AAN) assembled a panel of experts including epileptologists, general neurologists, and doctors in pharmacy with expertise in antiepileptic drugs. Panel members with expertise in obstetrics, obstetrical nursing, and teratology were also included.

The Quality Standards Subcommittee and Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and



American Epilepsy Society developed a set of clinical questions relevant to the evaluation of management issues related to the care of women with epilepsy (WWE) during pregnancy.

The strength of the practice recommendations was directly linked to the class of evidence using the scheme described in the "Rating Scheme for the Strength of the Recommendations" field.

### 2013 Reaffirmation

The AAN assesses their clinical practice guidelines every 2 years to determine whether new literature has been published that would warrant an update. The following steps are taken:

- Biennial correspondence is sent to all authors and the facilitator.
- An updated literature search and a review of methodological soundness are performed by a Guideline Development Subcommittee (GDS) member. (Note: The search should specifically seek to identify new evidence that would change the conclusions in the systematic review or recommendations in the CPG.)

All documents biennially reviewed by the GDS that don't require an update are reaffirmed. See the AAN [Clinical Practice Guideline Process Manual](#)  for additional information.

### 2016 Reaffirmation

A Guideline Development, Dissemination, and Implementation (GDDI) Subcommittee member who had expertise in epilepsy conducted a targeted literature search for high quality studies using the same criteria as presented in the original guideline. The GDDI reviewer and the subcommittee reviewed the new evidence and determined that the following three criteria were met: 1. There is no new evidence that would alter conclusions or recommendations in the guideline since the last literature search, 2. Guideline methodology is sound and current methodology is not substantially different, and 3. No significant practice variation relevant to the guideline currently exists.

## Rating Scheme for the Strength of the Recommendations

### Classification of Recommendations

The strength of practice recommendations is linked directly to the level of evidence:

Level A = Established as effective, ineffective, or harmful (or established as useful/predictive or not useful/predictive) for the given condition in the specified population. (Level A rating requires at least two consistent Class I studies.\*)

Level B = Probably effective, ineffective, or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified population. (Level B rating requires at least one Class I study or two consistent Class II studies.)

Level C = Possibly effective, ineffective, or harmful (or possibly useful/predictive or not useful/predictive) for the given condition in the specified population. (Level C rating requires at least one Class II study or two consistent Class III studies.)

Level U = Data inadequate or conflicting; given current knowledge, treatment (test, predictor) is unproven.

\*In exceptional cases, one convincing Class I study may suffice for an "A" recommendation if: 1) all criteria are met, 2) the magnitude of effect is large (relative rate improved outcome >5 and the lower limit of the confidence interval is >2).

## Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

## Method of Guideline Validation

External Peer Review

Internal Peer Review

## Description of Method of Guideline Validation

The Quality Standards Subcommittee and Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology (AAN) and American Epilepsy Society reviewed and approved a draft of the article. The draft was next sent to members of the Practice Committee of the AAN and American Epilepsy Society for further review and then to Neurology® for peer review. Boards of the AAN and American Epilepsy Society reviewed and approved the final version of the article. At each step of the review process, external reviewers' suggestions were explicitly considered. When appropriate, the expert panel made changes to the document.

The guideline was approved by the Quality Standards Subcommittee April 15, 2008; by the Therapeutics and Technology Assessment Subcommittee December 17, 2007; by the Practice Committee January 10, 2009; and by the AAN Board of Directors March 25, 2009.

## Evidence Supporting the Recommendations

### Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

## Benefits/Harms of Implementing the Guideline Recommendations

### Potential Benefits

Appropriate use of preconceptional folic acid, prenatal vitamin K, and antiepileptic drugs during pregnancy and breastfeeding in women with epilepsy

### Potential Harms

Not stated

## Qualifying Statements

### Qualifying Statements

This statement is provided as an educational service of the American Academy of Neurology (AAN). It is based on an assessment of current scientific and clinical information. It is not intended to include all possible proper methods of care for a particular neurologic problem or all legitimate criteria for choosing to use a specific procedure. Neither is it intended to exclude any reasonable alternative methodologies. The AAN recognizes that specific patient care decisions are the prerogative of the patient and the physician caring for the patient, based on all of the circumstances involved. The clinical context section is made available in order to place the evidence-based guideline(s) into perspective with current practice habits and challenges. No formal practice recommendations should be inferred. The findings and conclusions in the report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

## Implementation of the Guideline

### Description of Implementation Strategy

An implementation strategy was not provided.

## Implementation Tools

Foreign Language Translations

Patient Resources

Quick Reference Guides/Physician Guides

Resources

Slide Presentation

Staff Training/Competency Material

Wall Poster

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

## Institute of Medicine (IOM) National Healthcare Quality Report Categories

### IOM Care Need

Living with Illness

Staying Healthy

### IOM Domain

Effectiveness

Patient-centeredness

Safety

## Identifying Information and Availability

### Bibliographic Source(s)

Harden CL, Pennell PB, Koppel BS, Hovinga CA, Gidal B, Meador KJ, Hopp J, Ting TY, Hauser WA, Thurman D, Kaplan PW, Robinson JN, French JA, Wiebe S, Wilner AN, Vazquez B, Holmes L, Krumholz A, Finnell R, Shafer PO, Le Guen C. Practice parameter update: management issues for women with epilepsy--focus on pregnancy (an evidence-based review): vitamin K, folic acid, blood levels, and breastfeeding. Report of the Quality Standards Subcommittee [trunc]. *Neurology*. 2009 Jul 14;73(2):142-9. [45 references] [PubMed](#)

### Adaptation

Not applicable: The guideline was not adapted from another source.

### Date Released

2009 Jul (reaffirmed 2016)

## Guideline Developer(s)

American Academy of Neurology - Medical Specialty Society

American Epilepsy Society - Disease Specific Society

## Source(s) of Funding

American Academy of Neurology (AAN)

Development of this guideline was supported by The Milken Family Foundation.

## Guideline Committee

The Quality Standards Subcommittee and Therapeutics and Technology Assessment Subcommittee

## Composition of Group That Authored the Guideline

*Guideline Authors:* C.L. Harden, MD; P.B. Pennell, MD; B.S. Koppel, MD; C.A. Hovinga, PharmD; B. Gidal, PharmD; K.J. Meador, MD; J. Hopp, MD; T.Y. Ting, MD; W.A. Hauser, MD; D. Thurman, MD, MPH; P.W. Kaplan, MB, FRCP; J.N. Robinson, MD; J.A. French, MD; S. Wiebe, MD; A.N. Wilner, MD; B. Vazquez, MD; L. Holmes, MD; A. Krumholz, MD; R. Finnell, PhD; P.O. Shafer, RN, MN; C. Le Guen

## Financial Disclosures/Conflicts of Interest

The American Academy of Neurology (AAN) is committed to producing independent, critical and truthful clinical practice guidelines (CPGs). Significant efforts are made to minimize the potential for conflicts of interest to influence the recommendation of this CPG. To the extent possible, the AAN keeps separate those who have a financial stake in the success or failure of the products appraised in the CPGs and the developers of the guidelines. Conflict of interest forms were obtained from all authors and reviewed by an oversight committee prior to project initiation. AAN limits the participation of authors with substantial conflicts of interest. The AAN forbids commercial participation in, or funding of, guideline projects. Drafts of the guidelines have been reviewed by at least three AAN committees, a network of neurologists, Neurology peer reviewers, and representatives from related fields. The AAN Guideline Author Conflict of Interest Policy can be viewed at [www.aan.com](http://www.aan.com)

### Disclosure

The authors report the following conflicts of interest: Dr. Harden has served on the scientific advisory board of Cyberonics, GlaxoSmithKline, UCB Pharma, Valeant, and SK Pharmaceuticals and on the speakers' bureau of GlaxoSmithKline, Pfizer, UCB Pharma, and Abbott. She serves as an editor of *Epilepsy Currents* and receives publishing royalties from Elsevier. Dr. Harden has received research funding from Forest, UCB Pharma, Ortho McNeil, and NIH/NINDS. Dr. Harden sees women with epilepsy in her office practice. Dr. Pennell has served on the Expert Panel for the Keppra Pregnancy Registry sponsored by UCB Pharma. She has received funding for travel from the Northeast Regional Epilepsy Group for speaking at their 2008 Epilepsy Symposium, by the UK Research Council for speaking at the Epilepsy Research UK International Expert Workshop, by UCB Pharma for attending the Executive Panel meeting for the Pregnancy Registry, by the American Epilepsy Society for attending the Board of Directors' Meeting, by the Epilepsy Foundation for attending the Board of Directors' and orientation meetings, by the Long Island Jewish Hospital for lecturing at Neurology Grand Rounds, by Duke University for lecturing at Neurology Grand Rounds, by Brigham and Women's Hospital for lecturing at the Epilepsy Research Conference, by the Milken foundation for attending Pregnancy Registry meetings, and by Massachusetts General Hospital for speaking at the Annual Teratogens Course. She has received honoraria from Journal Watch Neurology for a contributing article, paid for by Massachusetts Medical Society, *NEJM*, for review for the *Lancet Neurology*, the Northeast Regional Epilepsy group for speaking at 2008 Epilepsy Symposium, North Shore Long Island Jewish Health system, Duke University, University of Maryland, the Massachusetts General Hospital for speaking at the postgraduate course in Human Teratogens, and the AAN for speaking and directing annual courses. Dr. Pennell has served as a contributing editor for *Epilepsy Currents* and is on the editorial board of *Epilepsia*. Dr. Pennell has received research support from UCB Pharma, Marinus Pharmaceuticals, NIH, NINDS, NIMH, CDC, and Emory University Research Council. Dr. Koppel reports no disclosures. Dr. Hovinga estimates less than 10% of his clinical effort is spent on pharmacology consults. Dr. Gidal has served on the scientific advisory board for GlaxoSmithKline, UCB Pharma, and Abbott Labs and served as an editor for *Epilepsy & Behavior*, *The*

*Annals of Pharmacotherapy*, and *Pharmacist's Letter*. Dr. Gidal has received research support from UCB Pharma. Dr. Meador serves as a journal editor for *Neurology*, *Journal of Clinical Neurophysiology*, *Cognitive and Behavioral Neurology*, *Epilepsy & Behavior*, *Epilepsy Currents*, and *Epilepsy.com*. He has received research funding from NIH/NINDS, GlaxoSmithKline, Eisai, Marius, Myriad, Neuropace, SAM Technology, and UCB Pharma. Dr. Meador estimates that 30–40% of his clinical effort is spent on EEGs and the clinical care of patients with epilepsy. Dr. Hopp receives royalties from UpToDate.com electronic medical journal. She has been on the speakers' bureau of UCB Pharma and GlaxoSmithKline. Dr. Hopp has given testimony in a medico-legal case. Dr. Ting served on the scientific advisory board of UCB Pharma and has received honoraria from the Epilepsy Foundation of America. Dr. Hauser has served on the scientific advisory board of Ovation and Valeant. He has served on the editorial board of *Acta Neurologica Scandinavica*, *Neuroepidemiology*, and *Epilepsy Research*. He has received honoraria from Cornell University Symposium on epilepsy and acted as a consultant to Pfizer. Dr. Hauser has received research support from AAMC/CDC, NIH/NINDS, FAA, Mayo Clinic, and Hotchkiss Neurological Institute, and has given expert testimony in his role as an FAA consultant. Dr. Thurman is an employee of the CDC. Dr. Kaplan has served on the speakers' bureau of UCB Pharma, GSK, and Ortho McNeil. He serves as an associate editor for *Neurophysiologie Clinique*, *Journal of Clinical Neurophysiology*, and *Epilepsia*. He receives royalties from Demos Publications for the books *Neurological Disease in Women*, *Epilepsy A to Z*, *Imitators of Epilepsy*, and *Nonconvulsive Status Epilepticus*. He has received speaker honoraria from Medical College of South Carolina, Duke University, and Medical College of Virginia, has received research funding from NIH, Schwarz, Ortho McNeil, and Pfizer, and has acted as a consultant for Schering-Plough and Infinite Biological Technologies. Dr. Robinson reports no disclosures. Dr. French has served on the scientific advisory board of UCB Pharma, Johnson and Johnson, Eisai, Novartis, Valeant, Icagen, Intranasal, Sepracor, and Marinus. She has received funding for travel to present findings or give lectures from UCB Pharma, Kyowa, Eisai, Johnson and Johnson, Valeant, and GlaxoSmithKline. She has served as an associate editor for *Epilepsy Currents* and supplement editor for *Epileptic Disorders*. Dr. French is the president of the Epilepsy Study Consortium, which receives money from multiple pharmaceutical companies (including GlaxoSmithKline, UCB Pharma, Johnson and Johnson, Cyberonics, Schwarz Pharma, Ortho McNeil, Eisai, Jazz Pharmaceuticals, Ovation Pharmaceuticals, Endo Pharmaceuticals, Bial Pharmaceuticals, Neurovista, Valeant Pharmaceuticals, Icagen, Supernus, Intranasal, SK Pharmaceuticals, Taro Pharmaceuticals, Neurotherapeutics, Sepracor, and Novartis) and she consults on behalf of the consortium. Dr. French has received research funding from Johnson and Johnson, Eisai, UCB Pharma, SK Pharmaceuticals, Valeant, Pfizer, NIH, and Epilepsy Research Foundation. Dr. Wiebe serves on the editorial board of *Neurology*, *Epilepsia*, *Epilepsy & Behavior*, and *Canadian Journal of Neurological Sciences*. Dr. Wilner has served on the scientific advisory board of and received funding for travel from GlaxoSmithKline. He receives royalties from Demos Publications for *Epilepsy: 199 Answers* and *Epilepsy in Clinical Practice*. He receives board of directors compensation from GlaxoSmithKline. Dr. Vazquez has served on the scientific advisory board of Eisai, UCB, GSK, and Ortho McNeil. She has received honoraria from UCB, GSK, OrthoMcNeil, and Eisai. Dr. Vazquez has served on a speakers' bureau for Eisai, GSK, Ortho McNeil, UCB, and Novartis. Dr. Holmes receives research support from Abbott Labs, Eisai, Novartis, Ortho McNeil, and Pfizer. Dr. Krumholz has served on the Department of Transportation Expert Panel on Commercial Drivers and Epilepsy and has served on the editorial board of *The Neurologist* and *Clinical EEG and Neuroscience*. He has received honoraria from the Robert Wood Johnson Medical School for grand rounds. Dr. Finnell has served on the scientific advisory board of the NEAD study at Emory University, the University of Houston Center for Life Sciences Technology, the NIH, and the NIEHS National Advisory Environmental Health Sciences Council. He has received funding for travel from Fundacion BBVA, NIEHS National Advisory Environmental Health Sciences Council, IKMC Steering Committee, European Epilepsy Meeting, NIH, and AES. Dr. Finnell has served as a journal editor for *Birth Defects Research Part A* and holds a patent on folate receptor autoantibody assay. He has received honoraria from McGill University-Montreal Neurological Institute and has received research funding from the Centers for Disease Control and Prevention for the National Birth Defects Prevention Study and the Methodist Hospital Research Institute. Dr. Finnell has given expert testimony, prepared affidavits, and acted as a witness regarding legal proceedings related to the topic of this manuscript. Ms. Shafer has served on the scientific advisory board for GlaxoSmithKline, has received funding for travel from the Epilepsy Therapy Project, and acts as a reviewer for *Epilepsy & Behavior* and *Epilepsia*. She has received honoraria from Medscape, American Epilepsy Society, and Cyberonics Nursing Advisory Board. Ms. Shafer is on the speakers' bureau of the Epilepsy Foundation of Massachusetts and Rhode Island, acts as a consultant to the Epilepsy Therapy Project, and is a contributing writer at *epilepsy.com*. Ms. Le Guen reports no disclosures.

## Guideline Endorser(s)

Child Neurology Society - Medical Specialty Society

## Guideline Status

This is the current release of the guideline.

The American Academy of Neurology reaffirmed the currency of this guideline in 2016.

This guideline meets NGC's 2013 (revised) inclusion criteria.

## Guideline Availability

Electronic copies: A list of American Academy of Neurology (AAN) guidelines, along with a link to a Portable Document Format (PDF) file for this guideline, is available at the [AAN Web site](#) .

Print copies: Available from the AAN Member Services Center, (800) 879-1960, or from AAN, 201 Chicago Avenue South, Minneapolis, MN 55415.

## Availability of Companion Documents

The following are available:

- Management issues for women with epilepsy—focus on pregnancy vitamin K, folic acid, blood levels, and breastfeeding. AAN summary of evidence-based guideline for clinicians. St. Paul (MN): American Academy of Neurology (AAN). 2009. 2 p. Available from the [AAN Web site](#) .
- Practice parameter update: management issues for women with epilepsy—focus on pregnancy (an evidence-based review): teratogenesis and perinatal outcomes. Case study. St. Paul (MN): American Academy of Neurology. 2009. 6 p. Available from the [AAN Web site](#) .
- Practice parameter update: management issues for women with epilepsy—focus on pregnancy (an evidence-based review): vitamin K, folic acid, blood levels, and breastfeeding. Wall poster. St. Paul (MN): American Academy of Neurology. 2009. 2 p. Available from the [AAN Web site](#) .
- Practice parameter update: management issues for women with epilepsy—focus on pregnancy (an evidence-based review). Slide presentation. St. Paul (MN): American Academy of Neurology. 2009. 105 p. Available from the [AAN Web site](#) .
- AAN guideline development process [online]. St. Paul (MN): American Academy of Neurology. Available from the [AAN Web site](#) .

## Patient Resources

The following are available:

- Women with epilepsy: drug risks and safety during pregnancy. AAN summary of evidence-based guideline for patients and their families. St. Paul (MN): American Academy of Neurology (AAN). 2009. 2 p. Electronic copies: Available in [English](#)  and [Spanish](#)  in Portable Document Format (PDF) from the AAN Web site.
- Women with epilepsy: drug risks to the fetus or baby during pregnancy. AAN summary of evidence-based guideline for patients and their families. St. Paul (MN): American Academy of Neurology (AAN). 2009. 1 p. Electronic copies: Available in [English](#)  and [Spanish](#)  in Portable Document Format (PDF) from the AAN Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

## NGC Status

This NGC summary was completed by ECRI Institute on December 4, 2009. The information was verified by the guideline developer on April 20, 2010. This summary was updated by ECRI Institute on April 13, 2011 following the U.S. Food and Drug Administration advisory on Topamax (topiramate). This summary was updated by ECRI Institute on July 10, 2013 following the U.S. Food and Drug Administration advisory on Valproate. The currency of the guideline was reaffirmed by the developer in 2013 and this summary was updated by ECRI Institute on May 27, 2015. The currency of the guideline was reaffirmed by the developer in 2016 and this summary was updated by ECRI Institute on January 18, 2017.

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